

U. S. Appln. No. 09/368,670
Supplemental Amendment

wherein R_{11a} is H; C_{1-10} alkyl; C_6 aryl; C_{7-10} alkylaryl; C_{3-7} cycloalkyl or C_{4-8} (alkylcycloalkyl) optionally substituted with carboxyl; or heterocycle- C_{1-6} alkyl;

and R_{11b} is C_{1-6} alkyl substituted with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl; or C_{7-16} aralkyl substituted on the aromatic portion with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl;

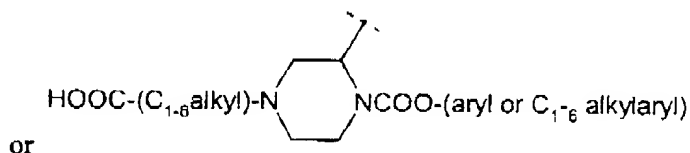
or R_{11a} and R_{11b} are joined to form a 3 to 7-membered nitrogen-containing ring optionally substituted with carboxyl or (C_{1-6} alkoxy) carbonyl;

or

b) when Q is N-Y, a is 0 or 1, b is 0 or 1, and

B is an acyl derivative of formula $R_{11}-C(O)-$ or a sulfonyl of formula $R_{11}-SO_2$ wherein

- R_{11} is (i) C_{1-10} alkyl optionally substituted with carboxyl or C_{1-6} alkanoyloxy; C_{1-6} alkoxy; or carboxyl substituted with 1 to 3 C_{1-6} alkyl substituents;
- (ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, both optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl;
- (iii) C_6 or C_{10} aryl or C_{7-16} aralkyl optionally substituted with C_{1-6} alkyl, hydroxy, or amino optionally substituted with C_{1-6} alkyl; or
- (iv) Het optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally substituted with C_{1-6} alkyl, or amido optionally substituted with C_{1-6} alkyl,



R_6 , when present, is C_{1-6} alkyl substituted with carboxyl;

R_5 , when present, is C_{1-6} alkyl optionally substituted with carboxyl;

and

c) when Q is either CH_2 or N-Y, then

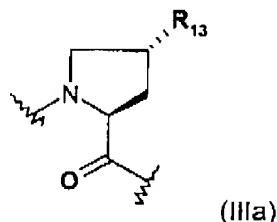
R_4 is C_{1-10} alkyl, C_{3-7} cycloalkyl or C_{4-10} (alkylcycloalkyl);

z is oxo or thioxo;

R_3 is C_{1-10} alkyl optionally substituted with carboxyl, C_{3-7} cycloalkyl or C_{4-10} (alkylcycloalkyl);

W is a group of formula IIIa:

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wherein R_{13} is o-tolylmethoxy; m-tolylmethoxy; p-tolylmethoxy; (4-tert-butyl)methoxy; (3I-Ph)CH₂O; (4Br-Ph)O; (2Br-Ph)O; (3Br-Ph)O; (4I-Ph)O; (3Br-Ph)CH₂O; (3,5-Br₂-Ph)CH₂O; or R_{13} is OR₁₂ or SR₁₂ wherein R_{12} is C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl or Het, all optionally substituted with C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₁₋₆ alkoxy, acetylamido, nitro, CF₃, NH₂, OH, SH, halo, carboxyl, carboxy(lower)alkyl or a second aryl or aralkyl;

R_{1a} is hydrogen, and R_1 is the side chain of an amino acid selected from the group consisting of cysteine (Cys), aminobutyric acid (Abu), norvaline (Nva) and allylglycine (AlGly); or

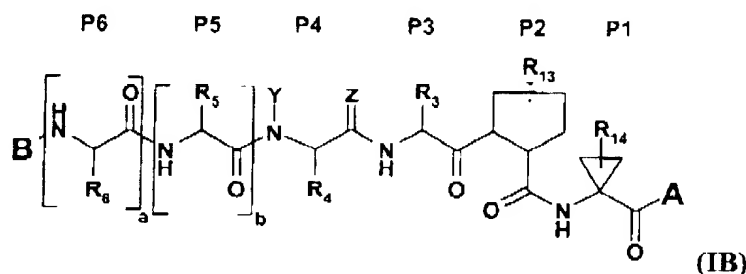
R_{1a} and R_1 together form a 3- to 6-membered ring optionally substituted with R_{14} wherein R_{14} is C₁₋₆ alkyl, C₃₋₅ cycloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆ aryl or C₇₋₁₀ aralkyl all optionally substituted with halo; and

A is hydroxy; or C₁₋₆ alkylamino, di(C₁₋₆ alkyl)amino or phenyl-C₁₋₆ alkylamino;

wherein Het is a five-, six-, or seven-membered saturated or unsaturated, including aromatic, heterocycle containing from one to four heteroatoms selected from nitrogen, oxygen and sulfur, which heterocycle is optionally fused to a benzene ring;

or a non-toxic salt or ester thereof.

47. (Twice Amended) A compound of formula IB:



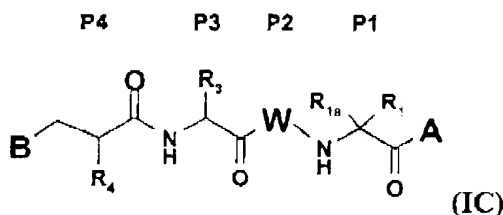
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F2
Amide
 wherein B is an acyl derivative of formula $R_{11}C(O)-$ wherein R_{11} is C_{1-6} alkyl; C_{1-6} alkoxy; C_{3-7} cycloalkyl optionally substituted with hydroxy; amido optionally substituted with C_{1-6} alkyl or Het; C_6 or C_{10} aryl, C_{7-16} aralkyl or Het all optionally substituted with C_{1-6} alkyl or hydroxy; a, b, R_6 , R_5 , Y, R_4 , Z, R_3 , and A are as defined in claim 1,

R_{13} is R_{12} , OR_{12} , $C(O)OR_{12}$, SR_{12} , NHR_{12} or $NR_{12}R_{12a}$ wherein R_{12} and R_{12a} are as defined in claim 1; and

R_{14} is C_{1-6} alkyl, C_{2-6} alkenyl optionally substituted with halogen; C_{6-10} aryl or C_{7-10} aralkyl optionally substituted with halogen; or a non-toxic salt or ester thereof.

F3
 68. (Twice Amended) A compound of formula IC:



wherein B is an amide of formula $R_{11a}N(R_{11b})C(O)-$ wherein R_{11a} is C_{1-6} alkyl; C_{3-6} cycloalkyl; C_{3-7} (alkylcycloalkyl) optionally substituted with carboxy; C_{1-3} carboxyalkyl; C_6 aryl; C_{7-10} arylalkyl; 2-tetrahydrofuranylmethyl; or 2-thiazolidylmethyl; and R_{11b} is C_{1-4} alkyl substituted with carboxyl;

R_4 , R_3 , W, R_{1a} , R_1 , and A are as defined in claim 1.

REMARKS

It has been discovered that certain substituent groups in claims 27, 47 and 68 lack antecedent basis in certain claims from which these three claims depend; specifically, certain groups in the R_{12} definition in claim 27, the R_{11} definition in claim 47, and the R_{11a} definition in claim 68. Claims 27, 47 and 68 have therefore been amended to place these claims into independent form to obviate